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FORM PTO-1449 INFORMATION DISCLOSURE STATEMENT	ATTY. DOCKET NO. 0609.4350001/REF/KKV	APPLICATION NO. 09/380,704
	APPLICANT BUSH <i>et al.</i>	
	FILING DATE September 8, 1999	GROUP To be assigned 1647

U.S. PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE
BBB	AA1	5,242,932	09/07/1993	Gandy <i>et al.</i>	514	313	12/17/1991
	AB1	5,373,021	12/13/1994	Marangos	514	483	04/26/1993
	AC1	5,523,295	06/04/1996	Fasman	514	63	07/06/1994
	AD1	5,688,516	11/18/1997	Raad <i>et al.</i>	424	409	10/03/1994
	AE1	5,688,651	11/18/1997	Solomon	435	7.1	12/16/1994
	AF1	5,705,401	01/06/1998	Masters <i>et al.</i>	436	518	09/16/1994
	AG1	5,707,821	01/13/1998	Rydel <i>et al.</i>	435	18	06/07/1995
BBB	AH1	5,721,106	02/24/1998	Maggio <i>et al.</i>	435	7.8	09/12/1994

FOREIGN PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
BBB	A11	WO 92/18111	10/29/1992	WIPO			Yes No
BBB	AJ1	WO 93/10459	05/27/1993	WIPO			Yes No
BBB	AK1	WO 93/24451	12/09/1993	WIPO			Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

BBB	AL	1	Assaf, S.Y and Chung, S.-H., "Release of endogenous Zn ²⁺ from brain tissue during activity," <i>Nature</i> 308:734-736 (April 1984).
	AM	1	Atwood, C.S. <i>et al.</i> , "Dramatic Aggregation of Alzheimer AB by Cu(II) Is Induced by Conditions Representing Physiological Acidosis," <i>J. Biol. Chem.</i> 273:12817-12826 (May 1998).
	AN	1	Bacon, P.A. <i>et al.</i> , "Rheumatoid Disease, Amyloidosis and its Treatment with Penicillamine," <i>Eur. J. Rheum. Inflamm.</i> 2:70-74 (1979)
	AO	1	Barrow, C.J., and Zagorski, M.G., "Solution Structures of β Peptide and Its Constituent Fragments: Relation to Amyloid Deposition," <i>Science</i> 253:179-182 (July 1991).
BBB	AP	1	Barrow, C.J., <i>et al.</i> , "Solution Conformations and Aggregational Properties of Synthetic Amyloid β -Peptides of Alzheimer's Disease," <i>J. Mol. Biol.</i> 225:1075-1093 (June 1992).

EXAMINER <i>Bridget E. Bunner</i>	DATE CONSIDERED 11/4/03
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EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
BBB	A12	WO 94/04167	03/03/1994	WIPO			<input type="checkbox"/> Yes <input type="checkbox"/> No
BBB	AJ2	WO 95/31199	11/23/1995	WIPO			<input type="checkbox"/> Yes <input type="checkbox"/> No
BBB	AK2	WO 96/07096	03/07/1996	WIPO			<input type="checkbox"/> Yes <input type="checkbox"/> No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)			
BBB	AL	2	Basun, H., et al., "Metals and trace elements in plasma and cerebrospinal fluid in normal ageing and Alzheimer's disease," <i>J. Neurol. Transm. [P-D Sect.]</i> 3:231-258 (1991).
	AM	2	Behl, C., et al., "Hydrogen Peroxide Mediates Amyloid β Protein Toxicity," <i>Cell</i> 77:817-827 (June 1994).
	AN	2	Biaglow, J.E. and Kachur, A.V., "The Generation of Hydroxyl Radicals in the Reaction of Molecular Oxygen with Polyphosphate Complexes of Ferrous Ion," <i>Radiation Res.</i> 148:181-187 (August 1997).
	AO	2	Boado, R.J. et al., "Drug Delivery of Antisense Molecules to the Brain for Treatment of Alzheimer's Disease and Cerebral AIDS," <i>J. Pharm. Sci.</i> 87(11):1308-1315 (November 1998).
BBB	AP	2	Borman, S., "Diverse Strategies Emerge For Diagnosing Alzheimer's Disease," <i>Chem. Eng. News</i> 272:33-34 (June 1996).

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beb	A13	WO 96/12544	05/02/1996	WIPO			Yes No
beb	AJ3	WO 96/28471	09/19/1996	WIPO			Yes No
beb	AK3	WO 97/04794	02/13/1997	WIPO			Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

beb	AL	3	Bruce, A.J. <i>et al.</i> , "β-Amyloid toxicity in organotypic hippocampal cultures: Protection by EUK-8, a synthetic catalytic free radical scavenger," <i>Proc. Natl. Acad. Sci. USA</i> 93:2312-2316 (March 1996).
	AM	3	Burdick, D., <i>et al.</i> , "Assembly and Aggregation Properties of Synthetic Alzheimer's A4/β Amyloid Peptide Analogs," <i>J. Biol. Chem.</i> 267:546-554 (January 1992).
	AN	3	Burns, J.A., <i>et al.</i> , "Selective Reduction of Disulfides by Tris(2-carboxyethyl)phosphine," <i>J. Org. Chem.</i> 56:2648-2650 (April 1991).
	AO	3	Busciglio, J., and Yankner, B.A., "Apoptosis and increased generation of reactive oxygen species in Down's Syndrome neurons <i>in vitro</i> ," <i>Nature</i> 378:776-779 (December 1995).
beb	AP	3	Bush, A.I., <i>et al.</i> , "A Novel Zinc(II) Binding Site Modulates the Function of the BA4 Amyloid Protein Precursor of Alzheimer's Disease," <i>J. Biol. Chem.</i> 268:16109-16112 (August 1993).

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Budget C. Dunner

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BBB	A14	WO 97/09976	03/20/1997	WIPO			Yes No
BBB	AJ4	WO 97/36885	10/09/1997	WIPO			Yes No
BBB	AK4	WO 98/06403	02/19/1998	WIPO			Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

BBB	AL	4	Bush, A.I., et al., "Modulation of A β Adhesiveness and Secretase Site Cleavage by Zinc," <i>J. Biol. Chem.</i> 269:12152-12158 (April 1994).
	AM	4	Bush, A.I., et al., "The Amyloid β -Protein Precursor and Its Mammalian Homologues," <i>J. Biol. Chem.</i> 269:26618-26621 (October 1994).
	AN	4	Bush, A.I., et al., "Rapid Induction of Alzheimer A β Amyloid Formation by Zinc," <i>Science</i> 265:1464-1467 (September 1994).
	AO	4	Bush, A.I., et al., Response to "Zinc and Alzheimer's Disease," <i>Science</i> 268:1920-1923 (June 1995).
BBB	AP	4	Butterfield, D.A., et al., " β -Amyloid Peptide Free Radical Fragments Initiate Synaptosomal Lipoperoxidation in a Sequence-Specific Fashion: Implications to Alzheimer's Disease," <i>Biochem. Biophys. Res. Commun.</i> 200:710-715 (April 1994).

EXAMINER Bridget E. Bunner

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EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
<u>BOB</u>	AIS	WO 98/40071	09/17/1998	WIPO			<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<u>BOB</u>	AJS	WO 99/09981	03/04/1999	WIPO			<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
	AK						<input type="checkbox"/> Yes <input type="checkbox"/> No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)			
<u>BOB</u>	AL	<u>5</u>	Butterfield, D.A., et al., "AB(25-35) Peptide Displays H ₂ O ₂ -Like Reactivity Towards Aqueous Fe ²⁺ , Nitroxide Spin Probes, and Synaptosomal Membrane Proteins," <i>Life Sci.</i> 58:217-228 (1996).
	AM	<u>5</u>	Cherny, R.A. et al., "The Aggregation of AB in Human Brain is Mediated by Zinc," <i>Soc. for Neurosci. Abstracts</i> 23:534 (October 1997).
	AN	<u>5</u>	Chong, Y.-H., and Suh, Y.-H., "Aggregation of amyloid precursor proteins by aluminum in vitro," <i>Brain Research</i> 679:137-141 (January 1995).
	AO	<u>5</u>	Colaco, C.A.L.S., et al., "The role of the Maillard reaction in other pathologies: Alzheimer's disease," <i>Nephrol. Dial. Transplant.</i> 11(Suppl. 5):7-12 (1996).
<u>BOB</u>	AP	<u>5</u>	Connor, J.R. et al., "A Histochemical Study of Iron, Transferrin, and Ferritin in Alzheimer's Diseased Brains," <i>J. Neurosci. Res.</i> 31:75-83 (January 1992).

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	AK						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

BEB	AL	6	Connor, J.R. et al., "Ceruloplasmin levels in the human superior temporal gyrus in aging and Alzheimer's disease," <i>Neurosci. Lett.</i> 159:88-90 (September 1993).
	AM	6	Coyle, J.T., and Puttfarcken, P., "Oxidative Stress, Glutamate, and Neurodegenerative Disorders," <i>Science</i> 262:689-695 (October 1993).
	AN	6	Crapper McLachlan, D.R. et al., "Intramuscular desferrioxamine in patients with Alzheimer's disease," <i>Lancet</i> 337:1304-1308 (June 1991).
	AO	6	Guajungco, M.P. and Lees, G.J., "Zinc and Alzheimer's disease: is there a direct link?" <i>Brain Res. Rev.</i> 23:219-236 (April 1997).
BEB	AP	6	Dedman, D.J. et al., "Iron and aluminum in relation to brain ferritin in normal individuals and Alzheimer's-disease and chronic renal-dialysis patients," <i>Biochem J.</i> 287:509-514 (1992).

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	(This area is reserved for the filing of a request for a hearing or for a request for a review of the Commissioner's decision.)	

U.S. PATENT DOCUMENTS

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	AI						Yes No
	AJ						Yes No
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Deibel, M.A. et al., "Copper, iron, and zinc imbalances in severely degenerated brain regions in Alzheimer's disease: possible relation to oxidative stress," <i>J. Neurol. Sci.</i> 143:137-142 (November 1996).	AL	Z	
Doré, S., et al., "Insulin-like growth factor I protects and rescues hippocampal neurons against β -amyloid- and human amylin-induced toxicity," <i>Proc. Natl. Acad. Sci. USA</i> 94:4772-4777 (April 1997).	AM	Z	
Dryks, T. et al., "Amyloidogenicity of β A4 and β A4-bearing Amyloid Protein Precursor Fragments by Metal-catalyzed Oxidation," <i>J. Biol. Chem.</i> 267:18210-18217 (September 1992).	AN	Z	
Ehmann W.D. et al., "Brain Trace Elements in Alzheimer's Disease," <i>NeuroToxicology</i> 7:197-206 (1986).	AO	Z	
Esler, W.P., et al., "Zinc-Induced Aggregation of Human and Rat β -Amyloid Peptides In Vitro," <i>J. Neurochem.</i> 66:723-732 (February 1996).	AP	Z	

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	AI						Yes No
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BEB	AL	8	Esler, W.P., <i>et al.</i> , "A β deposition inhibitor screen using synthetic amyloid," <i>Nat. Biotechnol.</i> 15:258-263 (March 1997).
	AM	8	Fitzgerald, D.J., "Zinc and Alzheimer's Disease," <i>Science</i> 268:1920 (June 1995).
	AN	8	Folstein, M. "Nutrition and Alzheimer's Disease," <i>Nutrition Reviews</i> 55:23-25 (January 1997).
	AO	8	Fraser, P.E., <i>et al.</i> , "pH-dependent structural transitions of Alzheimer amyloid peptides," <i>Biophys. J.</i> 60:1190-1201 (November 1991).
BEB	AP	8	Frederikse, P.H., <i>et al.</i> , "Oxidative Stress Increases Production of β -Amyloid Precursor Protein and β -Amyloid (A β) in Mammalian Lenses, and A β Has Toxic Effects on Lens Epithelial Cells," <i>J. Biol. Chem.</i> 271:10169-10174 (April 1996).

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	AI						Yes No
	AJ						Yes No
	AK						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)			
BEB	AL	2	Frederickson, C.J., "Neurobiology of Zinc and Zinc-Containing Neurons," <i>Int. Rev. Neurobiol.</i> 31:145-238 (1989).
	AH	2	Frieden, E., "Ceruloplasmin: A Multi-functional Cupro-protein of Vertebrate Plasma," in: <i>Inflammatory Diseases and Copper</i> , Sorenson, J.R.J., ed., Clifton, N.J.: Humana Press, pp.159-169 (1982).
	AN	2	Giampaolo, V., "Copper and Inflammation," in: <i>Inflammatory Diseases and Copper</i> , Sorenson, J.R.J., ed., Clifton, N.J.: Humana Press, pp. 329-345 (1982).
	AD	2	Giulian, D. <i>et al.</i> , "Specific Domains of β -Amyloid from Alzheimer Plaque Elicit Neuron Killing in Human Microglia," <i>J. Neurosci.</i> 16:6021-6037 (October 1996).
BEB	AP	2	Glenner, G.G., and Wong, C.W., "Alzheimer's Disease: Initial Report of the Purification and Characterization of Novel Cerebrovascular Amyloid Protein," <i>Biochem. Biophys. Res. Commun.</i> 120: 885-890 (May 1984).

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Bob	AL	10	Golde, T.E., <i>et al.</i> , "Processing of the Amyloid Protein Precursor to Potentially Amyloidogenic Derivatives," <i>Science</i> 255:728-730 (February 1992).
	AM	10	Good, P.F. <i>et al.</i> , "Selective Accumulation of Aluminum and Iron in the Neurofibrillary Tangles of Alzheimer's Disease: A Laser Microprobe (LAMMA) Study," <i>Ann. Neurol.</i> 31:286-292 (March 1992).
	AN	10	Goodman, Y. <i>et al.</i> , "Nordihydroguaiaretic acid protects hippocampal neurons against amyloid β -peptide toxicity, and attenuates free radical and calcium accumulation," <i>Brain Res.</i> 654:171-176 (August 1994).
	AO	10	Goodman, Y., and Mattson, M.P., "Secreted Forms of β -Amyloid Precursor Protein Protect Hippocampal Neurons against Amyloid β -Peptide-Induced Oxidative Injury," <i>Exp. Neurol.</i> 128:1-12 (July 1994).
Bob	AP	10	Gorevic, P.D. <i>et al.</i> , "The Biological Significance of Amyloid," <i>Ann. New York Acad. Sci.</i> 389:380-394 (1982).

EXAMINER *Bridget E. Bunner*

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<div style="font-size: 2em;">BEB</div>	AL	11	Grundke-Iqbal, I. et al., "Ferritin is a component of the neuritic (senile) plaque in Alzheimer dementia," <i>Acta Neuropathol.</i> 81:105-110 (December 1990).				
	AM	11	Gutteridge, J.M.C., and Wilkins, S., "Copper Salt-Dependent Hydroxyl Radical Formation Damage to Proteins Acting as Antioxidants," <i>Biochim. Biophys. Acta</i> 759:38-41 (August 1983).				
	AN	11	Haass, C. et al., "Amyloid β -peptide is produced by cultured cells during normal metabolism," <i>Nature</i> 359:322-325 (September 1992).				
	AO	11	Haley, J.V., "Zinc Sulfate and Wound Healing," <i>J. Surg. Res.</i> 27:168-174 (September 1979).				
	AP	11	Halliwell, B., and Gutteridge, J.M.C., "Oxygen toxicity, oxygen radicals, transition metals and disease," <i>Biochem. J.</i> 219:1-14 (April 1984).				
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	AK						Yes No

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BOB	AL	12	Halliwel, B., "Reactive Oxygen Species and the Central Nervous System," <i>J. Neurochem.</i> 59:1609-1623 (November 1992).
	AM	12	Han, J., et al., "Quantitation of Hydrogen Peroxide Using Tris(2-carboxyethyl)phosphine," <i>Anal. Biochem.</i> 234:107-109 (February 1996).
	AN	12	Han, J.C., and Han, G.Y., "A Procedure for Quantitative Determination of Tris(2-carboxyethyl)phosphine, an Odorless Reducing Agent More Stable and Effective Than Dithiothreitol," <i>Anal. Biochem.</i> 220:5-10 (July 1994).
	AO	12	Hansen, M.B., et al., "Re-examination and further development of a precise and rapid dye method for measuring cell growth/cell kill," <i>J. Immunol. Meth.</i> 119:203-210 (May 1989).
BOB	AP	12	Herman, D., "Aging: A Theory Based on Free Radical and Radiation Chemistry," <i>J. Gerontology</i> 2:298-300 (July 1956).

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Bridget C. Bunner

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OTHER (Including Author, Title, Date, Pertinent Pages, etc.)							
BEB	AL	13	Harris, M.E., et al., "Direct Evidence of Oxidative Injury Produced by the Alzheimer's β -Amyloid Peptide (1-40) in Cultured Hippocampal Neurons," <i>Exp. Neurol.</i> 131:193-202 (February 1995).				
	AM	13	Hensley, K et al., "A model for beta-amyloid aggregation and neurotoxicity based on free radical generation by the peptide: Relevance to Alzheimer disease," <i>Proc. Natl. Acad. Sci. U.S.A.</i> 91:3270-3274 (April 1994).				
	AN	13	Hensley, K et al., "Brain Regional Correspondence Between Alzheimer's Disease Histopathology and Biomarkers of Protein Oxidation," <i>J. of Neurochem.</i> 65:2146-2156 (November 1995).				
	AO	13	Hensley, K., et al., "Reactive Oxygen Species as Causal Agents in the Neurotoxicity of the Alzheimer's Disease-Associated Amyloid Beta Peptide," <i>Ann N. Y. Acad. Sci.</i> 786:120-134 (1996).				
BEB	AP	13	Hesse, L., et al., "The β A4 amyloid precursor protein binding to copper," <i>FEBS Lett.</i> 349:109-116 (July 1994).				
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OTHER (Including Author, Title, Date, Pertinent Pages, etc.)							
<div style="font-size: 2em; font-family: cursive;">BBB</div>	AL	14	Hilbich, C., <i>et al.</i> , "Aggregation and Secondary Structure of Synthetic Amyloid BA4 Peptides of Alzheimer's Disease," <i>J. Mol. Biol.</i> 218:149-163 (March 1991).				
<div style="font-size: 4em; font-family: cursive;"> </div>	AM	14	Hilbich, C. <i>et al.</i> , "Substitutions of Hydrophobic Amino Acids Reduce the Amyloidogenicity of Alzheimer's Disease BA4 Peptides," <i>J. Mol. Biol.</i> 228:460-473 (November 1992).				
<div style="font-size: 4em; font-family: cursive;"> </div>	AN	14	Hsu, J.M., <i>et al.</i> , "Zinc Deficiency and Incorporation of ¹⁴ C-labeled Methionine into Tissue Proteins in Rats," <i>J. Nutrition</i> 99:425-432 (December 1969).				
<div style="font-size: 4em; font-family: cursive;"> </div>	AO	14	Huang, X. <i>et al.</i> , "Zinc-induced Alzheimer's AB1-40 Aggregation Is Mediated by Conformational Factors," <i>J. Biol. Chem.</i> 272:26464-26470 (October 1997).				
<div style="font-size: 2em; font-family: cursive;">BBB</div>	AP	14	Ida, N., <i>et al.</i> , "Analysis of Heterogeneous BA4 Peptides in Human Cerebrospinal Fluid and Blood by a Newly Developed Sensitive Western Blot Assay," <i>J. Biol. Chem.</i> 271:22908-22914 (September 1996).				
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BEB	AL	15	Jarrett, J.T., <i>et al.</i> , "The Carboxy Terminus of the β Amyloid Protein Is Critical for the Seeding of Amyloid Formation: Implications for the Pathogenesis of Alzheimer's Disease," <i>Biochem.</i> 32:4693-4697 (May 1993).
	AM	15	Jarrett, J.T., and Lansbury, Jr., P.T., "Amyloid Fibril Formation Requires a Chemically Discriminating Nucleation Event: Studies of an Amyloidogenic Sequence from the Bacterial Protein OsmB," <i>Biochem.</i> 31:12345-12352 (December 1992).
	AN	15	Johnstone, E.M. <i>et al.</i> , "Conservation of the sequence of the Alzheimer's disease amyloid peptide in dog, polar bear and five other mammals by cross-species polymerase chain reaction analysis," <i>Mol. Brain Res.</i> 10:299-305 (July 1991).
	AO	15	Joshi, J.G., "Iron and Aluminum Homeostasis in Neural Disorders," <i>Environ. Health Persp.</i> 102:207-213 (1994).
BEB	AP	15	Kang, J. <i>et al.</i> , "The precursor of Alzheimer's disease amyloid A4 protein resembles a cell-surface receptor," <i>Nature</i> 325: 733-736 (February 1987).

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BEB	AL	16	Kawahara, M. <i>et al.</i> , "Alzheimer's Disease Amyloid β -Protein Forms Zn^{2+} -Sensitive, Cation-Selective Channels Across Excised Membrane Patches from Hypothalamic Neurons," <i>Biophys. J.</i> 73:67-75 (July 1997).
	AN	16	Kennard, M.L. <i>et al.</i> , "Serum levels of the iron binding protein p97 are elevated in Alzheimer's disease," <i>Nat. Med.</i> 2:1230-1235 (November 1996).
	AN	16	Kidani, Y. <i>et al.</i> , "Mass spectrometry of 5-chloro-7-iodo-8-quinolinol metal chelates," <i>Jpn. Analyst</i> 23:1375-1378 (1974).
	AO	16	Kirschner, D.A. <i>et al.</i> , "Synthetic peptide homologous to β protein from Alzheimer disease forms amyloid-like fibrils <i>in vitro</i> ," <i>Proc. Natl. Acad. Sci. USA</i> 84:6953-6957 (October 1987).
BEB	AP	16	Kirshenbaum, K., and Daggett, V., "pH-Dependent Conformations of the Amyloid β (1-28) Peptide Fragment Explored Using Molecular Dynamics," <i>Biochem.</i> 34:7629-7639 (June 1995).

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Bob	AL	<u>17</u>	Kisilevsky, R., "Inflammation-Associated Amyloidogenesis," <i>Mol. Neurobiol.</i> 8:65-66 (February 1994).				
	AM	<u>17</u>	Koh, J.Y., and Choi, D.W., "Quantitative determination of glutamate mediated cortical neuronal injury in cell culture by lactate dehydrogenase efflux assay," <i>J. Neurosci. Meth.</i> 20:83-90 (May 1987).				
	AN	<u>17</u>	Kotaki, H., <i>et al.</i> , "Intestinal Absorption and Metabolism of Cloiquinol in the Rat," <i>J. Pharm. Dyn.</i> 6:881-887 (November 1983).				
	AO	<u>17</u>	Kuo, Y.-M., <i>et al.</i> , "Water-soluble A β (N-40, N-42) Oligomers in Normal and Alzheimer Disease Brains," <i>J. Biol. Chem.</i> 271:4077-4081 (February 1996).				
Bob	AP	<u>17</u>	Landers, J.W., and Zak, B., "Determination of Serum Copper and Iron in a Single Small Sample," <i>Am. J. Clin. Pathol.</i> 29:590-592 (June 1958).				

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OTHER (Including Author, Title, Date, Pertinent Pages, etc.)			
<i>BBB</i>	AL	<u>18</u>	Lindeman, R.D., <i>et al.</i> , "Myocardial zinc metabolism in experimental myocardial infarction," <i>J. Lab. Clin. Med.</i> 81:194-204 (February 1973).
<i> </i>	AM	<u>18</u>	Lockhart B.P. <i>et al.</i> , "Inhibitors of free radical formation fail to attenuate direct beta-amyloid ₂₅₋₃₅ peptide-mediated neurotoxicity in rat hippocampal cultures," <i>J. Neurosci. Res.</i> 39:494-505 (November 1994).
<i> </i>	AN	<u>18</u>	Lohr, J.B., "Oxygen Radicals and Neuropsychiatric Illness," <i>Arch. Gen. Psychiatry</i> 48:1097-1106 (December 1991).
<i> </i>	AO	<u>18</u>	Maggio, J.E., <i>et al.</i> , "Zinc and Alzheimer's Disease," <i>Science</i> 268:1920-1921 (June 1995).
<i>BBB</i>	AP	<u>18</u>	Mantyh, P.W., <i>et al.</i> , "Aluminum, Iron, and Zinc Ions Promote Aggregation of Physiological Concentrations of β -Amyloid Peptide," <i>J. Neurochem.</i> 61:1171-1174 (September 1993).

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	AI						Yes No
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OTHER (Including Author, Title, Date, Pertinent Pages, etc.)			
<u>BEB</u>	AL	19	Markesbery, W.R., "Oxidative Stress Hypothesis in Alzheimer's Disease," <i>Free Rad. Biol. Med.</i> 23:134-147 (1997).
<u>BEB</u>	AM	19	Masters, C.L., et al., "Amyloid plaque core protein in Alzheimer disease and Down syndrome," <i>Proc. Natl. Acad. Sci. USA</i> 82:4245-4249 (June 1985).
<u>BEB</u>	AN	19	Masters, C. L. et al., "Neuronal origin of a cerebral amyloid: neurofibrillary tangles of Alzheimer's disease contain the same protein as the amyloid of plaque cores and blood vessels," <i>EMBO J.</i> 4:2757-2763 (November 1985).
	AO	19	Maury, C.P.J., "Biology of Disease: Molecular Pathogenesis of β-Amyloidosis in Alzheimer's Disease And Other Cerebral Amyloidoses," <i>Lab. Invest.</i> 72:4-16 (January 1995).
<u>BEB</u>	AP	19	McGeer, P.L., and McGeer, E.G., "The inflammatory response system of brain: implications for therapy of Alzheimer and other neurodegenerative diseases," <i>Brain Res. Rev.</i> 21:195-218 (September 1995).

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BEB	AL	20	Mecocci, P., M.D. <i>et al.</i> , "Oxidative Damage to Mitochondrial DNA Shows Marked Age-dependent Increases in Human Brain," <i>Ann. Neurol.</i> 34:609-616 (October 1993).
	AM	20	Menkin, V., "Studies on Inflammation. X. The Cytological Picture of an Inflammatory Exudate in Relation to its Hydrogen Ion Concentration," <i>Am. J. Pathol.</i> 10:193-210 (March 1934).
	AN	20	Michikawa, M., <i>et al.</i> , "Oxygen Radical-Induced Neurotoxicity in Spinal Cord Neuron Cultures," <i>J. Neurosci. Res.</i> 37:62-70 (January 1994).
	AO	20	Milanino, R., <i>et al.</i> , "Copper and the Inflammatory Process," <i>Advances in Inflammation Research</i> 1:281-291 (1979).
BEB	AP	20	Moir, R.D. <i>et al.</i> , "Relative Increase in Alzheimer's Disease of Soluble Forms of Cerebral A β Amyloid Protein Precursor Containing the Kunitz Protease Inhibitory Domain," <i>J. Biol. Chem.</i> 273:5013-5019 (February 1998).

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Bridget E. Bunnell

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BBB	AL	21	Mok, S.S., <i>et al.</i> , "A Novel Metalloprotease in Rat Brain Cleaves the Amyloid Precursor Protein of Alzheimer's Disease Generating Amyloidogenic Fragments," <i>Biochemistry</i> 36:156-163 (January 1997).
	AM	21	Multhaup, G., <i>et al.</i> , "Interaction between the zinc(II) and the heparin binding site of the Alzheimer's disease β A4 amyloid precursor protein (APP)," <i>FEBS Lett.</i> 355:151-154 (November 1994).
	AN	21	Multhaup, G., <i>et al.</i> , "The Amyloid Precursor Protein of Alzheimer's Disease in the Reduction of Copper(II) to Copper(I)," <i>Science</i> 271:1406-1409 (March 1996).
	AO	21	Münch, G., <i>et al.</i> , "Advanced glycation endproducts in ageing and Alzheimer's disease," <i>Brain Res. Rev.</i> 23:134-143 (February 1997).
BBB	AP	21	Okada, H. <i>et al.</i> , "Effects of Metal-Containing Drugs Taken Simultaneously with Clotioquinol Upon Clinical Features of SMON," <i>J. Toxicol. Sci.</i> 9:327-341 (1984).

EXAMINER Bridget E. Dunner

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Bob	AL	22	Owen, C.A., Jr., "Uptake of ⁶⁴ Cu by Ceruloplasmin In Vitro (38878)," <i>Proc. Soc. Exp. Biol. Med.</i> 149:681-682 (July 1975).				
	AM	22	Padmanabhan, G., et al., "Clioquinol," in: <i>Analytical Profiles of Drug Substances</i> , Volume 18, Florey, K., ed., Academic Press, Inc.: San Diego, CA, pp. 57-90 (1989).				
	AN	22	Pérez, A.A. et al., "Alzheimer Amyloids Aβ1-40 and Aβ1-42 are Differentially Degraded by Insulin Degrading Enzyme (IDE) From Human Brain," <i>Soc. Neurosci. Abstracts</i> 23:821 (October 1997).				
	AO	22	Peters, G., and Rodgers, M.A.J., "Single-Electron Transfer from NADH Analogues to Singlet Oxygen," <i>Biochim. Biophys. Acta</i> 637:43-52 (August 1981).				
Bob	AP	22	Pierce, J.E.S., et al., "Immunohistochemical Characterization of Alterations in the Distribution of Amyloid Precursor Proteins and β-Amyloid Peptide after Experimental Brain Injury in the Rat," <i>J. Neurosci.</i> 16:1083-1090 (February 1996).				

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

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	AL	23	Potempa, L.A., et al., "Effect of Divalent Metal Ions and pH upon the Binding Reactivity of Human Serum Amyloid P Component, a C-reactive Protein Homologue, for Zymosan," <i>J. Biol. Chem.</i> 260:12142-12147 (October 1985).				
	AM	23	Richardson, J.S., et al., "On the Possible Role of Iron-Induced Free Radical Peroxidation in Neural Degeneration in Alzheimer's Disease," <i>Ann. N.Y. Acad. Sci.</i> 648:326-327 (1992).				
	AN	23	Roberts, G.W., et al., "BA4 amyloid protein deposition in brain after head trauma," <i>Lancet</i> 338:1422-1423 (December 1991).				
	AO	23	Robinson, S.R. et al., "Most amyloid plaques contain ferritin-rich cells," <i>Alzheimer's Res.</i> 1:191-196 (1995).				
	AP	23	Rogers, J., et al., "Clinical trial of indomethacin in Alzheimer's disease," <i>Neurology</i> 43:1609-1611 (August 1993).				

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	FILING DATE September 8, 1999	GROUP To be assigned 1647

U.S. PATENT DOCUMENTS							
EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE
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EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
	AI						Yes No
	AJ						Yes No
	AK						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)							
BOB	AL	24	Rohrer, A.E., et al., "Morphology and Toxicity of AB-(1-42) Dimer Derived from Neuritic and Vascular Amyloid Deposits of Alzheimer's Disease," <i>J. Biol. Chem.</i> 271:20631-20635 (August 1996).				
	AM	24	Rumble, B. et al., "Amyloid A4 Protein and Its Precursor in Down's Syndrome and Alzheimer's Disease," <i>New Eng. J. of Med.</i> 320:1446-1452 (June 1989).				
	AN	24	Sadowski, M. et al., "Astrocyte and microglia reaction in Alzheimer's disease in the hippocampal formation- a quantitative analysis," <i>Alzheimer's Res.</i> 1:71-76 (1995).				
	AO	24	Sano, M., et al., "A Controlled Trial of Selegiline, Alpha-Tocopherol, or Both as Treatment for Alzheimer's Disease," <i>N.Engl. J. Med.</i> 336:1216-1222 (April 1997).				
BOB	AP	24	Sayre, L.M., "Alzheimer's Precursor Protein and the Use of Bathocuproine for Determining Reduction of Copper(II)," <i>Science</i> 274:1933-1934 (December 1996).				

EXAMINER <i>Bridget E. Burner</i>	DATE CONSIDERED 11/4/03
EXAMINER: Initial reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.	

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	AI						Yes No
	AJ						Yes No
	AK						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)							
	AL	25	Schnabel, J., "New Alzheimer's Therapy Suggested," <i>Science</i> 260:1719-1720 (June 1993).				
BOB	AM	25	Schubert, D., and Chevion, M., "The Role of Iron in Beta Amyloid Toxicity," <i>Biochem. Biophys. Res. Commun.</i> 216:702-707 (November 1995).				
	AN	25	Selkoe, D.J., "Cell Biology of the Amyloid B-protein Precursor and the Mechanism of Alzheimer's Disease," <i>Ann. Rev. Cell Biol.</i> 10:373-403 (1994).				
	AO	25	Seubert, P. et al., "Isolation and quantification of soluble Alzheimer's β -peptide from biological fluids," <i>Nature</i> 359:325-327 (September 1992).				
BOB	AP	25	Shiraki, H., "Neuropathological aspects of the etiopathogenesis of subacute myelo-optico-neuropathy (SMON)," in <i>Handbook of Clinical Neurology. Intoxications of the Nervous System Part II</i> , Vinken, P. J. and Bruyn, G. W., eds., North-Holland Publishing Company, Amsterdam, Holland, pp.141-198 (1979).				

EXAMINER <i>Bridget E. Burner</i>	DATE CONSIDERED <i>11/4/03</i>
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FORM PTO-1449 INFORMATION DISCLOSURE STATEMENT		ATTY. DOCKET NO. 0609.4350001/REF/KKV		APPLICATION NO. 09/380,704	
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EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
	AI						Yes No
	AJ						Yes No
	AK						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)				
✓	<i>BEB</i>	AL	26	Shivers B.D. et al., "Alzheimer's disease amyloidogenic glycoprotein: expression pattern in rat brain suggests a role in cell contact," <i>EMBO J.</i> 7:1365-1370 (1988).
		AH	26	Shoji, M. et al., "Production of the Alzheimer Amyloid β Protein by Normal Proteolytic Processing," <i>Science</i> 258:126-129 (October 1992).
		AH	26	Sisodia, S.S. et al., "Cellular and molecular biology of Alzheimer's disease and animal models," <i>Neurodegenerative Diseases</i> 5:59-68 (February 1995).
		AO	26	Skinner, M. et al., "Observations on the amyloid-degrading activity of serum and its relationship to human neutrophil elastase," <i>Chem. Abst.</i> 101:453, Abstract No. 101:208677n (December 1984).
	<i>BEB</i>	AP	26	Smalheiser, H.R., and Swanson, D.R., "Indomethacin and Alzheimer's disease," <i>Neurology</i> 46:583 (February 1996).

EXAMINER <i>Bridget E. Bunner</i>	DATE CONSIDERED <i>11/4/03</i>
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FORM PTO-1449 <u>INFORMATION DISCLOSURE STATEMENT</u>	ATTY. DOCKET NO. 0609.4350001/REF/KKV	APPLICATION NO. 09/380,704
	APPLICANT BUSH et al.	
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	AI						Yes
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	AJ						Yes
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	AK						Yes
							No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)			
beb	AL	27	Smith, C. et al., "The molecular pathology of Alzheimer's disease: are we any closer to understanding the neurodegenerative process?," <i>Neuropathol. Appl. Neurobiol.</i> 20:322-38 (August 1994).
	AM	27	Smith, M.A., et al., "Radical AGEing in Alzheimer's disease," <i>Trends Neurosci.</i> 18:172-176 (April 1995).
	AN	27	Smith M.A., et al., "Iron accumulation in Alzheimer disease is a source of redox-generated free radicals," <i>Proc. Natl. Acad. Sci. U.S.A.</i> 94:9866-9868 (September 1997).
	AO	27	Sobue, I., "Clinical aspects of subacute myelo-optico-neuropathy (SMON)," in <i>Handbook of Clinical Neurology. Intoxications of the Nervous System Part II</i> , Vinken, P. J. and Bruyn, G. W., eds., North-Holland Publishing Company, Amsterdam, Holland, pp.115-139 (1979).
beb	AP	27	Soto, C. et al., "β-sheet breaker peptides inhibit fibrillogenesis in a rat brain model of amyloidosis: Implications for Alzheimer's therapy," <i>Nature Med.</i> 4:822-826 (July 1998).

EXAMINER Bridget C. Bunner	DATE CONSIDERED 11/4/03
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FORM PTO-1449 INFORMATION DISCLOSURE STATEMENT	ATTY. DOCKET NO. 0609.4350001/REF/KKV	APPLICATION NO. 09/380,704
	APPLICANT BUSH <i>et al.</i>	
	FILING DATE September 8, 1999	GROUP To be assigned 1647

U.S. PATENT DOCUMENTS							
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	AI						Yes
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	AJ						Yes
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	AK						Yes
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OTHER (Including Author, Title, Date, Pertinent Pages, etc.)			
BOB	AL	28	Soto, C., <i>et al.</i> , "Structural Determinants of the Alzheimer's Amyloid β -Peptide," <i>J. Neurochem.</i> 63:1191-1198 (October 1994).
	AM	28	Stankovic, A., and Mitrovic, D.R., "Aluminum Salts Stimulate Luminol-Enhanced Chemiluminescence Production by Human Neutrophils," <i>Free Rad. Res. Comms.</i> 14:47-55 (1991).
	AN	28	Tanzi, R.E. <i>et al.</i> , "The Wilson disease gene is a copper transporting ATPase with homology to the Menkes disease gene," <i>Nat. Gen.</i> 5:344-350 (December 1993).
	AO	28	Tanzi, R.E. <i>et al.</i> , "Amyloid β Protein Gene: cDNA, mRNA Distribution, and Genetic Linkage Near the Alzheimer Locus," <i>Science</i> 235:880-884 (February 1987).
BOB	AP	28	Tamura, Z., "Clinical Chemistry of Clloquinol," <i>Jpn. J. Med. Sci. Biol.</i> 28:69-77 (1975).

EXAMINER <i>Bridget C. Dunner</i>	DATE CONSIDERED 11/4/03
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FORM PTO-1449				ATTY. DOCKET NO. 0609.4350001/REF/KKV		APPLICATION NO. 09/380,704	
INFORMATION DISCLOSURE STATEMENT				APPLICANT BUSH et al.			
				FILING DATE September 8, 1999		GROUP To be assigned 11647	
U.S. PATENT DOCUMENTS							
EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE
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EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
	AI						Yes
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	AJ						Yes
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	AK						Yes
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OTHER (Including Author, Title, Date, Pertinent Pages, etc.)							
BEB	AL	29	Tateishi, J. et al., "Strain-differences in dogs for neurotoxicity of clioquinol," <i>Lancet</i> 1:1289-1290 (June 1972).				
	AM	29	Tateishi, J. et al., "Myeloneuropathy in dogs induced by iodoxyquinoline," <i>Neurology</i> 22:702-709 (July 1972).				
	AN	29	Tateishi, J. et al., "Autoradiographic Distribution of ¹³¹ I-Clioquinol in Canine and Feline," <i>Folia Psychiatrica et Neurologica Japonica</i> 26:159-164 (1972).				
	AO	29	Tateishi, J. et al., "Experimental Myelo-optic Neuropathy Induced by Clioquinol," <i>Acta neuropath. (Berl.)</i> 24:304-320 (1973).				
	AP	29	Tateishi, J. et al., "Neurotoxicity of Clioquinol. Part III: Autoradiographic Distribution of Radioactive Clioquinol in Several Species of Animals," <i>Psychiat. Neurol. Jap.</i> 75:187-196 (1973).				
EXAMINER Bridget E. Bunner					DATE CONSIDERED 11/4/03		
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		APPLICANT BUSH et al.			
		FILING DATE September 8, 1999		GROUP To be assigned 1647	

U.S. PATENT DOCUMENTS							
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	AI						Yes
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OTHER (Including Author, Title, Date, Pertinent Pages, etc.)			
BEB	AL	30	Tateishi, J. et al., "Neurotoxicity of Clloquinol in Laboratory Animals," <i>Lancet</i> 2:1095 (November 1972).
	AM	30	Teller, J.K., et al., "Presence of soluble amyloid β -peptide precedes amyloid plaque formation in Down's Syndrome," <i>Nature Med.</i> 2:93-95 (January 1996).
	AN	30	Terhune, M.W., and Sandstead, H.H., "Decreased RNA Polymerase Activity in Mammalian Zinc Deficiency," <i>Science</i> 177:68-69 (July 1972).
	AO	30	Thomas, T., et al., " β -Amyloid-mediated vasoactivity and vascular endothelial damage," <i>Nature</i> 380:168-171 (March 1996).
BEB	AP	30	Tomiyama, T., et al., "Rifampicin Prevents the Aggregation and Neurotoxicity of Amyloid β Protein In Vitro," <i>Biochem. Biophys. Res. Comm.</i> 204:76-83 (October 1994).

EXAMINER Bridget E. Bunner	DATE CONSIDERED 11/4/03
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FORM PTO-1449 INFORMATION DISCLOSURE STATEMENT	ATTY. DOCKET NO. 0609.4350001/REF/KKV	APPLICATION NO. 09/380,704
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	FILING DATE September 8, 1999	GROUP To be assigned 1647

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	AI						Yes
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	AJ						Yes
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	AK						Yes
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OTHER (Including Author, Title, Date, Pertinent Pages, etc.)			
Bob	AL	31	Tomiyama, T., <i>et al.</i> , "Inhibition of Amyloid β Protein Aggregation and Neurotoxicity by Rifampicin," <i>J. Biol. Chem.</i> 271:6839-6844 (March 1996).
	AM	31	Thompson, C.M. <i>et al.</i> , "Regional Brain Trace-Element Studies in Alzheimer's Disease," <i>Neurotoxicol.</i> 9:1-8 (1988).
	AN	31	Tomski, S.J., and Murphy, R.M., "Kinetics of Aggregation of Synthetic β -Amyloid Peptide," <i>Arch. Biochem. Biophys.</i> 294:630-638 (May 1992).
	AO	31	Treuhart, P.S., and McCarty, D.J., "Synovial Fluid pH, Lactate, Oxygen and Carbon Dioxide Partial Pressure in Various Joint Diseases," <i>Arth. Rheum.</i> 4:475-484 (July-August 1971).
Bob	AP	31	Van Nostrand, W.E., "Zinc (II) Selectively Enhances the Inhibition of Coagulation Factor XIa by Protease Nexin-2/Amyloid β -Protein Precursor," <i>Thrombosis Res.</i> 78:43-53 (April 1995).

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FORM PTO-1449 <u>INFORMATION DISCLOSURE STATEMENT</u>	ATTY. DOCKET NO. 0609.4350001/REF/KKV	APPLICATION NO. 09/380,704
	APPLICANT BUSH <i>et al.</i>	
	FILING DATE September 8, 1999	GROUP To be assigned <i>647</i>

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	AI						Yes
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	AJ						Yes
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	AK						Yes
							No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)			
<i>beb</i>	AL	<u>32</u>	Warren, P.J. <i>et al.</i> , "The Distribution of Copper in Human Brain," <i>Brain</i> , 83:709-717 (1960).
	AM	<u>32</u>	Weismann, K., and Knudsen, L., "Effects of Penicillamine and Hydroxyquinoline on Absorption of Orally Ingested ⁶⁵ Zinc in the Rat," <i>J. Invest. Dermatol.</i> 71:242-244 (October 1978).
	AN	<u>32</u>	Wood, S.J., <i>et al.</i> , "Physical, Morphological and Functional Differences between pH 5.8 and 7.4 Aggregates of the Alzheimer's Amyloid Peptide A β ," <i>J. Mol. Biol.</i> 256:870-877 (March 1996).
	AO	<u>32</u>	Yates, C.M., <i>et al.</i> , "Enzyme Activities in Relation to pH and Lactate in Postmortem Brain in Alzheimer-Type and Other Dementias," <i>J. Neurochem.</i> 55:1624-1630 (November 1990).
<i>beb</i>	AP	<u>32</u>	Zagorski, M.G., and Barrow, C.J., "NMR Studies of Amyloid β -Peptides: Proton Assignments, Secondary Structure, and Mechanism of an α -Helix \rightarrow β -Sheet Conversion for a Homologous, 28-Residue, N-Terminal Fragment," <i>Biochemistry</i> 31:5621-5631 (June 1992).

EXAMINER <i>Bridget E. Bunner</i>	DATE CONSIDERED <i>11/4/03</i>
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	APPLICANT BUSH <i>et al.</i>	
	FILING DATE September 8, 1999	GROUP To be assigned 1647

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	AI						Yes
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	AJ						Yes
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	AK						Yes
							No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)							
BeB	AL	33	Beal, M. F., "Energy, Oxidative Damage, and Alzheimer's Disease: Clues to the Underlying Puzzle," <i>Neurobiol. Aging</i> 15:S171-S174 (1994).				
/	AM	33	Linert, W. <i>et al.</i> , "Dopamine, 6-hydroxydopamine, iron, and dioxygen-their mutual interaction and possible implication in the development of Parkinson's disease," <i>Biochim. Biophys. Acta</i> 1316:160-168 (August 1996).				
/	AN	33	Markesbery, W.R. and Ehmann, W.D., "Brain Trace Elements in Alzheimer Disease," Chapter 22 in <i>Alzheimer Disease</i> , Terry, R.D. <i>et al.</i> , eds., Raven Press, Ltd., New York (1994).				
BeB	AO	33	Soto, C. <i>et al.</i> , "Inhibition of Alzheimer's Amyloidosis by Peptides That Prevent β -Sheet Conformation," <i>Biochem. Biophys. Res. Comm.</i> 226:672-680 (September 1996).				
	AP						

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FORM PTO-1449

FIRST SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

ATTY. DOCKET NO.
0609.4350001/REF/KKV

APPLICATION NO.
09/380,704

APPLICANT
BUSH et al.

FILING DATE
September 8, 1999

GROUP
To be assigned 1647

U.S. PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE
BEB	AA2	5,357,636	10/25/1994	Dresdner, Jr. et al.	2	161.7	06/30/1992
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	AJ						Yes No
	AK						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AL		
	AM		
	AN		
	AO		
BEB	AP	33	Nakada, Y. and I.L. Kwee, "Guanidinoethane sulfate: brain pH alkaline shifter," <i>NeuroReport</i> 4:1035-1038 (August 1993)

EXAMINER Bridget C. Bunner

DATE CONSIDERED 11/4/03

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FORM PTO-1449

FIRST SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

ATTY. DOCKET NO.
0609.4350001/REF/KKV

APPLICATION NO.
09/380,704

APPLICANT
BUSH *et al.*

FILING DATE
September 8, 1999

GROUP
To be assigned 1147

U.S. PATENT DOCUMENTS

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	AI						Yes No
	AJ						Yes No
	AK						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

<i>bed</i>	AL	34	Schrader-Fischer, G. and P.A. Paganetti, "Effect of alkalizing agents on the processing of the β -amyloid precursor protein," <i>Brain Research</i> 716:91-100 (April 1996)
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EXAMINER *Bridget C. Bunner*

DATE CONSIDERED 11/4/03

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FORM PTO-1449				ATTY. DOCKET NO. 0609.4350001		APPLICATION NO. 09/380,704	
SECOND SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT				APPLICANT Bush et al.			
				102 (e) DATE June 6, 2000		GROUP 1636 1647	
U.S. PATENT DOCUMENTS							
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EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
	AI						Yes No
	AJ						Yes No
	AK						Yes No
OTHER (Including Author, Title, Date, Pertinent Pages, etc.)							
	AL	34					
BeB	AM	34	Atwood, C.S. et al., "Copper-Mediated Aggregation And Polymerization of Aβ," Soc. Neurosci. Abstr. 23:1883 (October 1997).				
	AN	34	Bruijn, L.I., et al., "ALS-Linked SOD1 Mutant G85R Mediates Damage to Astrocytes and Promotes Rapidly Progressive Disease with SOD1-Containing Inclusions," Neuron. 18:327-338 (February 1997).				
	AO	34	Ceballos-Picot, I., et al., "Peripheral Antioxidant Enzyme Activities And Selenium In Elderly Subjects And In Dementia Of Alzheimer's Type--Place Of The Extracellular Glutathione Peroxidase," Free Radic. Biol. Med. 20:579-587 (1996).				
BeB	AP	34	Chan, C.-W., et al., "Anti-apoptotic action of Alzheimer Aβ," Alzheimer's Reports 2:113-119 (March 1999).				
EXAMINER <u>Bridget E. Bunner</u>					DATE CONSIDERED <u>11/4/03</u>		
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FORM PTO-1449 SECOND SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT		ATTY. DOCKET NO. 0609.4350001		APPLICATION NO. 09/380,704	
102 (e) DATE June 6, 2000		GROUP 1616 1647			

U.S. PATENT DOCUMENTS							
EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE
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FOREIGN PATENT DOCUMENTS							
EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
	AI						Yes No
	AJ						Yes No
	AK						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)			
BOB	AL	35	Cohen, A.S., "Amyloidosis," <u>Arthritis and Allied Conditions: A Textbook of Rheumatology</u> , D.J. McCarty, ed., Lea and Febiger, Philadelphia, pp. 1273-1293 (1989).
	AM	35	Garzon-Rodriguez, W., et al., "Soluble Amyloid A β -(1-40) Exists as a Stable Dimer at Low Concentrations," <u>J. Biol. Chem.</u> 272:21037-21044 (August 1997).
	AN	35	Goto, J.J., et al., "Reactions of Hydrogen Peroxide with Familial Amyotrophic Lateral Sclerosis Mutant Human Copper-Zinc Superoxide Dismutases Studied by Pulse Radiolysis," <u>J. Biol. Chem.</u> 273:30104-30109 (November 1998).
	AO	35	Huang, X., et al., "The A β Peptide of Alzheimer's Disease Directly Produces Hydrogen Peroxide through Metal Ion Reduction," <u>Biochemistry</u> 38:7609-7616 (June 1999).
BOB	AP	35	Kisilevsky, R., "Amyloidosis: A Familial Problem in the Light of Current Pathogenetic Developments," <u>Lab. Invest.</u> 49:381-390 (October 1983).

EXAMINER <u>Bridget E. Bunner</u>	DATE CONSIDERED <u>11/4/03</u>
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FORM PTO-1449 SECOND SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT	ATTY. DOCKET NO. 0609.4350001	APPLICATION NO. 09/380,704
	APPLICANT Bush et al.	
	102(e) DATE June 6, 2000	GROUP 1616 1647

U.S. PATENT DOCUMENTS							
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EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
	AI						Yes No
	AJ						Yes No
	AK						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)							
BeB	AL	36	Kuo, Y.-M., et al., "High Levels of Circulating Aβ42 Are Sequestered by Plasma Proteins in Alzheimer's Disease," <i>Biochem. Biophys. Res. Commun.</i> 257:787-791 (April 1999).				
	AM	36	Lovell, M.A., et al., "Copper, iron and zinc in Alzheimer's disease senile plaques," <i>J. Neurol. Sci.</i> 158:47-52 (June 1998).				
	AN	36	Martins, R.N., et al., "Increased Cerebral Glucose-6-Phosphate Dehydrogenase Activity in Alzheimer's Disease May Reflect Oxidative Stress," <i>J. Neurochem.</i> 46:1042-1045 (April 1986).				
	AO	36	Kang, J., et al., "The precursor of Alzheimer's disease amyloid A4 protein resembles a cell-surface receptor," <i>Nature</i> 325:733-736 (February 1987).				
BeB	AP	36	Munomura, A., et al., "RNA Oxidation is a Prominent Feature of Vulnerable Neurons in Alzheimer's Disease," <i>J. Neurosci.</i> 19:1959-1964 (March 1999).				

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FORM PTO-1449 SECOND SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT		ATTY. DOCKET NO. 0609.4350001		APPLICATION NO. 09/380,704	
APPLICANT Bush et al.		102 (e) DATE June 6, 2000		GROUP 1647	

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	AI						Yes No
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	AK						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)			
<div style="font-size: 2em; font-family: cursive;">BEB</div>	AL	37	Pepys, M.B. and Baltz, M.L., "Acute Phase Proteins with Special Reference to C-Reactive Protein and Related Proteins (Pentaxins) and Serum Amyloid A Protein," in <u>Advances in Immunology</u> , Vol. 34, pp.141-212 (1983).
<div style="font-size: 2em; font-family: cursive;"> </div>	AM	37	Raby, C.A., et al., "Traumatic Brain Injury Increases β -Amyloid Peptide 1-42 in Cerebrospinal Fluid," <u>J. Neurochem.</u> 71:2505-2509 (December 1998).
<div style="font-size: 2em; font-family: cursive;"> </div>	AN	37	Rosen, D., et al., "Mutations in Cu/Zn superoxide dismutase gene are associated with familial amyotrophic lateral sclerosis," <u>Nature</u> 362:59-62 (March 1993).
<div style="font-size: 2em; font-family: cursive;"> </div>	AO	37	Smith, M. A., et al., "Oxidative damage in Alzheimer's," <u>Nature</u> 382:120-121 (July 1996).
<div style="font-size: 2em; font-family: cursive;">BEB</div>	AP	37	Suzuki, N., et al., "An Increased Percentage of Long Amyloid β -Protein Secreted by Familial Amyloid β -Protein Precursor (BAPP ₇₇) Mutants," <u>Science</u> 264:1336-1340 (May 1994).

EXAMINER Bridget C. Burner	DATE CONSIDERED 11/4/03
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FORM PTO-1449 SECOND SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT		ATTY. DOCKET NO. 0609.6350001		APPLICATION NO. 09/380,704	
		APPLICANT Bush et al.			
		102 (e) DATE June 6, 2000		GROUP 1647 1647	

U.S. PATENT DOCUMENTS							
EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE
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FOREIGN PATENT DOCUMENTS							
EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
	AI						Yes No
	AJ						Yes No
	AK						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)							
BOB	AL	38	Terry, R.D., et al., "Physical Basis of Cognitive Alterations in Alzheimer's Disease: Synapse Loss is the Major Correlate of Cognitive Impairment," <i>Ann. Neurol.</i> 30:572-580 (October 1991).				
	AM	38	Uchida, K. and Kawakishi, S., "Identification of oxidized Histidine Generated at the Active Site of Cu,Zn-Superoxide Dismutase Exposed to H ₂ O ₂ . Selective Generation Of 2-Oxo-Histidine At The Histidine 118," <i>J. Biol. Chem.</i> 269:2405-2410 (January 1994).				
	AN	38	Molozin, B., et al., "Participation of presenilin 2 in Apoptosis: Enhanced Basal Activity Conferred by an Alzheimer Mutation," <i>Science</i> 274:1710-1713 (December 1996).				
	AO	38	Yankner, B.A., et al., "Neurotrophic and Neurotoxic Effects of Amyloid β Protein: Reversal by Tachykinin Neuropeptides," <i>Science</i> 250:279-282 (October 1990).				
BOB	AP	38	Yim, M.B., et al., "A gain-of-function of an amyotrophic lateral sclerosis-associated Cu,Zn-superoxide dismutase mutant: An enhancement of free radical formation due to a decrease in K _m for hydrogen peroxide," <i>Proc. Natl. Acad. Sci. USA</i> 93:5709-5714 (June 1996).				

EXAMINER Bridget C. Dunner	DATE CONSIDERED 11/4/03
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FORM PTO-1449 <u>INFORMATION DISCLOSURE STATEMENT</u>	ATTY. DOCKET NO. 0609.4350001/JAG/KKV	APPLICATION NO. 09/380,704
	APPLICANT Bush et al.	
	102(e) Date June 6, 2000	GROUP 1646 1647

U.S. PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE
	AA2						
	AB2						
BBB	AC2	5,110,493	05/05/1992	Cherng-Chyi et al.	514	413	—
BBB	AD2	5,466,680	11/14/1995	Rudy	514	57	—
	AE						
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	AH						
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FOREIGN PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
	AL						Yes No
	AM						Yes No
	AN						Yes No
	AO						Yes No
	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

OTHER (including Author, Title, Date, Volume/Pages, Etc.)			
BEB	AO	32	Gutierrez-Correa, J. and A.O.M. Stoppani, Free Rad. Res. 22(3): 239-250 (March 1995) (publisher: Harwood Academic Publishers GmbH)
BEB	AP	39	Lodemann, E., Naturwissenschaften 66(9): 462-466 (September 1979) (publisher: Springer-Verlag)
BEB	AL	40	Sue, Y.-J. et al., Annals of Emergency Medicine 24(4): 709-712 (October 1994) (publisher: American College of Emergency Physicians)

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FORM PTO-1449				ATTY. DOCKET NO. 0609.4350001		APPLICATION NO. 09/380,704	
THIRD SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT				APPLICANT Bush et al.			
				102 (e) DATE June 6, 2000		GROUP 164 1647	

U.S. PATENT DOCUMENTS							
EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE
BOB	AA						
	AB2	5,927,283	07/27/1999	Abraham et al.	128	898	05/08/1997
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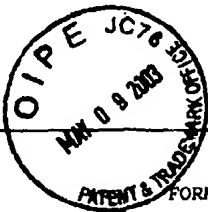
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EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
	AI						Yes No
	AJ						Yes No
BOB	AK5	WO 99/18432	04/15/1999	WIPO			Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)			
BOB	AL	39	Atwood, C.S. et al., "Role of Free Radicals and Metal Ions in the Pathogenesis of Alzheimer's Disease," in <i>Metal Ions in Biological Systems</i> , Sigel, A. and Sigel H., eds., Vol. 36, Ch. 10, Marcel Dekker Inc., New York, pp. 309-364 (1999).
BOB	AM	39	McKeon-O'Mally, C., et al., "Potential Therapeutic Targets for Alzheimer's Disease," <i>Emerging Therapeutic Targets</i> 2:157-179, Ashley Publications Ltd. (1998).
	AN	39	International Search Report for PCT/US80/11715, mailed August 30, 2000.
	AO		
	AP		

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FORM PTO-1449 SEVENTH SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT	ATTY. DOCKET NO. 0609.4350001/JAG/FRC	APPLICATION NO. 09/380,704
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	\$ 102(e) Date: June 6, 2000	GROUP 1647

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U.S. PATENT DOCUMENTS							
EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE
	AA						
	AB						
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	AH2	4,419,365	12/06/1983	McLachlan			12/21/1981

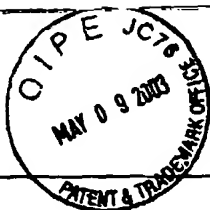
FOREIGN PATENT DOCUMENTS							
EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
beb	AI6	DE 40 04 978 A1	08/22/1991	Germany	—	—	Yes No
beb	AJ6	WO 94/27594 A2	12/08/1994	WIPO	—	—	Yes No
beb	AK6	WO 96/39144 A1	12/12/1996	WIPO	—	—	Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AR		
beb	AS	40	BIOMOL Product Data for TPEN, Catalog No. AP-300, Lot No. P3707, BIOMOL Research Laboratories, Inc. Plymouth Meeting, PA (July 2002)
beb	AT	40	Cardelli, M., et al., "Chelation Therapy. Unproved Modality in the Treatment of Alzheimer-Type Dementia," J. Am. Geriatr. Soc. 33:548-551, Blackwell Science (1985)

EXAMINER <i>Bridget E. Bunner</i>	DATE CONSIDERED <i>11/4/03</i>
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FORM PTO-1449 SEVENTH SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT	ATTY. DOCKET NO. 0609.4350001/JAG/FRC	APPLICATION NO. 09/380,704
	APPLICANT BUSH et al.	
	§ 102(e) Date: June 6, 2000	GROUP 1647

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U.S. PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE
BBB	AA3	5,310,936	05/10/1994	Regtop et al.			01/15/1992
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FOREIGN PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
BBB	AI7	WO 97/01559 A1	01/16/1997	WIPO			Yes No
	AJ						Yes No
	AK						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

BBB	AR	41	Ishii, T., and Bannai, S., "The Synergistic Action of the Copper Chelator Bathocuproine Sulphonate and Cysteine in Enhancing Growth of L1210 Cells In Vitro," J. Cell. Physiol. 125:151-155, Alan R. Liss, Inc. (1985)
BBB	AS	41	Kruck, T.P.A., et al., "Suppression of deferoxamine mesylate treatment-induced side effects by coadministration of isoniazid in a patient with Alzheimer's disease subject to aluminum removal by ionspecific chelation," Clin. Pharmacol. Ther. 48:439-446, Mosby-Year Book (1990)
BBB	AT	41	The Merck Index: An encyclopedia of chemicals, drugs, and biologicals, 11 th edition, Budavari, S., et al., eds., Merck & Co., Inc., Rahway, N.J., p. 9586 (1989)

EXAMINER: <u>Budget E. Bunner</u>	DATE CONSIDERED: <u>11/4/03</u>
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	\$ 102(e) Date: June 6, 2000	GROUP 1647

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	AI						Yes No
	AJ						Yes No
	AK						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

<i>Bob</i>	AR	42	Van Reyk, D.M., and Dean, R.T., "The Iron-selective Chelator Desferal Can Reduce Chelated Copper," <i>Free Radic. Res.</i> 24:55-60, Harwood Academic Publishers GmbH (January 1996)
	AS	42	Dieses File 351, Accession No. 8749401, Derwent WPI English language abstract for DE 4004978.
	AT		

EXAMINER <i>Bridget E. Gurner</i>	DATE CONSIDERED <i>11/4/03</i>
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